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TINEA CAPITIS TREATED WITH GRISEOFULVIN.

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Following the report of the successful use of oral griseofulvin in tinea capitis (Williams *et al.*, 1958) it was decided to treat all children admitted to the Ringworm Unit of Goldie Leigh Hospital by this method.

Thirty-one children were treated. Treatment was successful in all cases and there have been no subsequent relapses, the shortest period of follow up after apparent cure being two months. Further details are given in Table I. As can be seen from this table, the predominant infecting fungus was *Microsporum audouini*. There were four cases of *Microsporum canis* infection and one each with *Trichophyton rubrum*, *Trichophyton discoides* and *Trichophyton violaceum*. The child with *Trichophyton rubrum* infection of the scalp, which appeared clinically to be an endothrix infection, showed no other evidence of *Trichophyton rubrum* infection nor did the other members of her family.

Method of Treatment.

The antibiotic was given in doses ranging from 0·125 g. twice daily for younger children to 0·25 g. thrice daily for older children. No local treatment was given and the antibiotic was continued until most of the infected hairs showed a normal zone proximal to the infected part (Fig. 1). This took three to four weeks in most cases. At this stage the hair of the affected regions was clipped off close to the scalp. The children were examined daily after this and any remaining infected stumps removed manually when sufficient normal hair had grown to make it possible to pluck out the complete hair. One child was treated for seven days only, as it was considered that once a sufficient barrier to further fungus growth had been established in the newly formed hair keratin, further administration of the antibiotic might be unnecessary. Treatment was successful in this case (Case 2), but as several relapses occurred just afterwards in

children treated for longer periods this short course was not used again. Nevertheless, it may in future be found that a much shorter period of treatment is necessary, perhaps with a heavier loading dose of the antibiotic.

Results of Treatment.

All the children were cured. Details are given in Table I. The children were followed up for not less than two months after they were considered free from infection and unlikely to relapse before they were finally pronounced cured.

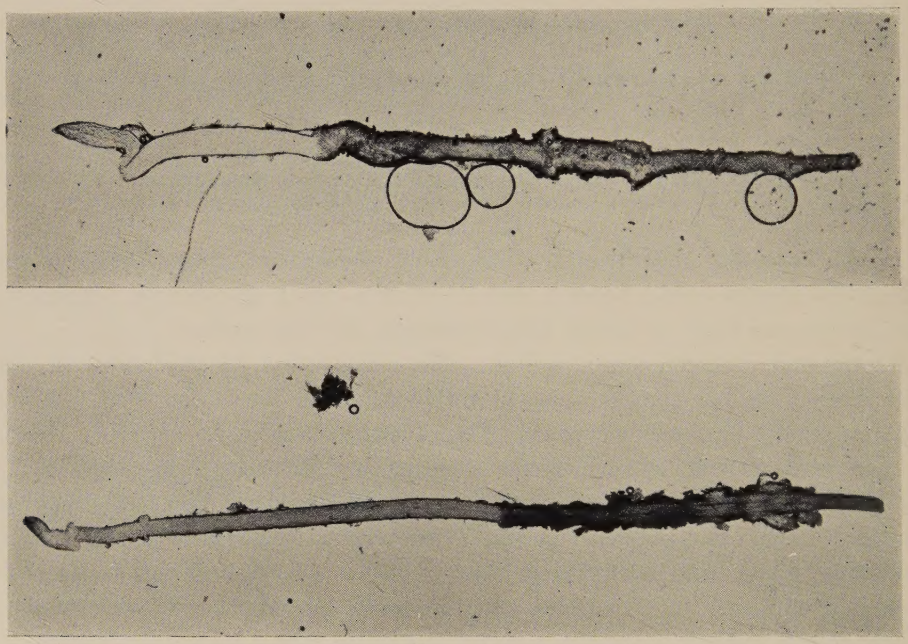

Fig. 1.

Three children relapsed some weeks after showing no evidence of infection but responded again to a second course of griseofulvin and were cured. The new areas of infected hairs were in different sites from the original ones but were due to the same fungus.

One child showed no changed in the appearance of his scalp ringworm five weeks after starting griseofulvin. Nevertheless, lesions of the glabrous skin healed. Three weeks after a second course of griseofulvin was started, normal hair growth was visible and after clipping the areas no further evidence of infection developed.

Two children continued to show infected stumps throughout the first course of treatment although most of the infected hair regrew normally. One of these children was treated by manual epilation and eventually healed. The other

TABLE I.—*Clinical Details.*

Case No.	Sex	Age in years	Infecting fungus	Clinical details	Daily dose of griseofulvin (g.)	Duration of first course in weeks	Result	Duration of second course in weeks	Result	Period of follow-up in months
1	F	7	*M. audouini*	Four patches. Relapsed after X-ray epilation, 26.iv.58	0·75	3	Cured	—	—	4
2	M	7		One large patch. X-ray epilation, Dec. 1957		1		—	—	5
3	F	3½	*M. canis*	Non-inflammatory ringworm. X-ray epilation for *M. audouini* infection, July 1957		4		—	—	4
4	F	3½		Several large patches	0·375	3	Relapsed 4 weeks after stopping treatment	3	Cured	3
5	M	1		Very extensive scalp ringworm		4	Cured	—	—	3
6	F	5		Large patches on scalp and legs		4		—	—	5
7	F	6½	*M. audouini*	Numerous small patches on scalp	0·75	1½	Relapsed 4 weeks after stopping treatment	3	Cured	3
8	M	2		Very extensive ringworm of scalp	0·375	4	Cured	—	—	3
9	M	6		One large patch on scalp	0·75	4		—	—	3
10	M	4		Several patches on scalp	0·375	4	Some infected stumps persisted	3	Cured	3
11	F	2		One large patch on scalp	0·375	4	Cured	—	—	3
12	M	7½	*Trichophyton rubrum*	One crusted patch on scalp, studded with pustules		3		—	—	5
13	M	6	*M. canis*	Several patches of inflammatory ringworm		4	Some infected stumps persisted	3	Cured	3
14	M	6		One large inflamed patch on scalp		4	Cured	—	—	2
15	M	7	*M. audouini*	One small inflamed patch on scalp		3		—	—	2
16	M	12	*Trichophyton discoides*	Numerous kerions on scalp and face		3		—	—	2
17	F	5½	*Trichophyton violaceum*	One scaly patch on vertex	0·75	4	Relapsed 3 weeks after stopping treatment	4	Cured	3
18	M	6		Several large patches on scalp		3	Cured	—	—	2
19	M	10		Several patches on scalp		3		—	—	2
20	M	8½		Numerous patches on scalp, face and legs		4		—	—	2
21	M	10½		Large patch on scalp		4	Cured. Some infected stumps continued to appear up to 3 weeks after stopping treatment	—	—	2
22	M	8	*M. audouini*	Isolated fluorescent stumps throughout scalp		3		—	—	2
23	M	2		One large patch on scalp and several small patches	0·25	4		—	—	3
24	M	7		One patch on scalp	0·375	4		—	—	2
25	M	5		One very large patch on scalp		4		—	—	2
26	F	5		One small patch on scalp		4		—	—	2
27	F	3		Several patches of scalp ringworm		4		—	—	2
28	M	5½			0·25	4	Cured	—	—	3
29	M	7		Very extensive scalp ringworm		5		—	—	2
30	M	8				5		—	—	2
31	M	8	*M. canis*	One patch on right temple	0·375	5		—	—	2
						3		—	—	2

child was treated with a second course of griseofulvin because infected stumps were becoming more numerous. During the second course, all the stumps showed normal hair growth and were satisfactorily removed leading to cure.

The type of fungus did not appear to influence the response to treatment although where fluorescence was absent, it was more difficult to judge when to clip the hair.

The one example of *Trichophyton discoides* infection showed very inflamed lesions which rather unexpectedly subsided rapidly during griseofulvin therapy and took a much shorter time to heal than previous experience with such kerions led one to expect.

Side Effects.

All the children appeared to tolerate the treatment very well. No side effects were apparent during the period of treatment apart from two cases of depression of the absolute polymorphonuclear leucocyte count.

Regular white cell counts and haemoglobin estimations were performed but the variation in the levels before starting treatment was so great that it was very difficult to interpret changes occurring during treatment. Nevertheless, there appeared to be a fairly regular drop in the total polymorphonuclear leucocyte count after starting griseofulvin, which rose again during the first week or so of treatment. The two cases of more severe depression of the polymorphonuclear leucocyte count occurred in children having a second course of treatment. In one child (Case 10) the total count fell from 4350 to 650 per cu. mm., while in the other (Case 7) the fall was from 3250 to 1400. These children were having a relatively large dose for their age. Apart from the low white cell counts, the children appeared normal. The polymorph counts rose to within normal limits a few days after stopping the antibiotic. After these blood changes had been observed, the dose of griseofulvin was halved so that the daily dose for a young child was 0·25 g. and for an older child 0·375 g. No further polymorph depression was noted.

Summary.

Thirty-one children with tinea capitis due to different types of fungus were treated with oral griseofulvin. All were cured although in a few cases a second course of treatment was necessary. In two children the polymorphonuclear leucocyte count fell to abnormally low levels but rose again within a few days of stopping the antibiotic.

I wish to thank the Matron of the Goldie Leigh Hospital and the nursing staff of the Ringworm Unit for their devoted work in the care of these patients. I wish to acknowledge the help given by Glaxo Limited and particularly their kindness in supplying me with griseofulvin.

Reference

Williams, D. I., Marten, R. H. and Sarkany, I. (1958) *Lancet*, ii, 1212.

THE TREATMENT OF FAVUS WITH GRISEOFULVIN.

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WHEREAS favus is extremely rare in Denmark, it is endemic in the Arctic regions of Greenland (Lomholt, 1959). Even there, the incidence is relatively low. The disease occurs exclusively in districts where the climate is unfavourable, and where the population lives or has until recently lived in turf houses. Under these circumstances, the possibility of rooting out the disease have so far been small, as there is no access to mycological analysis, x-ray epilation, or other technical aids. The results of treatment with ointment are poor, and there is, accordingly, the risk of spread to others, even adults (Inman, 1954). Internal treatment with griseofulvin is believed to be practicable even under these difficult circumstances. With this object in view, eight favus patients from Greenland have been submitted to experimental treatment.

Griseofulvin was isolated in 1939 by Oxford, Raistrick and Simonart. Gentles and Lauder and O'Sullivan in 1958 demonstrated its effectiveness in the treatment of trichophytosis in animals. The first attempts to treat humans were made by Williams, Marten and Sarkany (1958). Blank and Roth (1959), among others, showed that the activity of *Trichophyton schoenleini* was inhibited for 72 hours by griseofulvin in a concentration of 0·2–0·4 μg./ml. Degos, Rivalier and Leport (1959) and Esteves and Neves (1959) have reported clinical cure of favus after 27 days' treatment in 5 cases and 35 days' in 4 cases.

INVESTIGATION.

At the initiative of the Greenland Department, eight patients with favus from the Umanak district in Northern Greenland stayed in the Finsen Institute from 19 July to 9 October 1959.

Case 1.—A boy aged 8 years, son of a fisherman. His parents and four siblings were healthy. They lived in a one-roomed turf-covered wooden house. He had had crusts in the scalp for 6 months, and has been submitted to treatment with ointment in hospital.

The scalp was covered by embedded crusts, granulating wounds and atrophic scars. There were two red spots on the right cheek, one of which had a grey crust 2 mm. thick.

Case 2.—A man aged 18 years, a sealer. Three siblings (including Cases 7 and 8) suffered from favus. His father and four other siblings were healthy. His mother was dead. They lived in a turf house. Crusts in the scalp since the age of 6 years. Treated with ointment in hospital.

The crown of the head was bald, surrounded by coin-sized crusts embedded in skin. There was a small red spot at the nape of the neck and one on the left cheek.

Case 3.—A woman aged 22 years, daughter of a sealer. Her parents and four siblings were healthy. They lived in a one-roomed turf house. Crusts in the scalp since the age of 7 years. Treated four times with ointment in hospital.

The crown of the head was bald, surrounded by crusts embedded in the skin. The nails of the toes were thick, but not crumbling.

Case 4.—A woman aged 24 years, daughter of a sealer. A younger brother, who is now healthy, was treated for a similar disease in 1955. Her parents and three other siblings were healthy. They lived in a one-roomed wooden house. Crusts in the scalp since the age of 8 years. Treated with ointment both in hospital and at home.

The crown of the head was bald with a few red, follicular infiltrations. Embedded crusts along the hair margin. A few scaly spots on the back. The toe nails were thick, but not crumbling.

Case 5.—A boy aged 11 years, son of a sealer. A male cousin had favus. His parents were healthy. They lived in a one-roomed turf house. His siblings were away from home. Crusts in the scalp for the past year. Treated with ointment at home.

Thick hair with small, atrophic scars on the vertex and coin-sized crusts scattered over the crown.

Case 6.—A girl aged 17 years, a housemaid. Her parents and five siblings were healthy. She lived in a turf house during childhood, but later came to live in a wooden house with two rooms. Crusts in the scalp since the age of 8 years, treated with ointment in hospital.

Long, thick hair with nits 8-15 cm. above the skin. On the crown, ramifying, narrow scars, with embedded crusts in between. A red spot on the right cheek. The nails were thin and fragile.

Case 7.—A man aged 20 years, a sealer (brother of Cases 2 and 8). His mother was dead. His father and four other siblings were healthy. They lived in a one-roomed turf house. Crusts in the scalp from the age of 5 years, treated with ointment in hospital.

The crown was bald and surrounded by coin-sized crusts embedded in the skin. The nails of the index fingers were loose and thickened. The toe nails were thick and crumbling.

Case 8.—A woman aged 24 years, wife of a sealer (sister of Cases 2 and 7). Her mother was dead. Her father and four siblings were healthy. She lived in a small turf house during childhood, but since marriage has lived in a roomy wooden house. Crusts in the scalp since the age of 6 years.

The crown was bald. Along the hair margin there were small crusts embedded in the skin. On the back she had pale, oval spots with finely flaking borders. The nails of both thumbs and the right first toe were thickened and crumbling.

Each patient was submitted to careful general medical examination before the commencement of the treatment, with special emphasis on the detection of tuberculosis, venereal disease, parasitic affections, intestinal infection and nutritional disorders. No tuberculosis and neither intestinal infection nor infestation was demonstrated. Gonorrhoea in four patients and pediculosis in one were treated before starting griseofulvin.

Moderate anaemia, raised E.S.R., and raised gamma-globulin concentration in the serum were demonstrated in all the patients, presumably due to their diet having been deficient in vitamins, but rich in fats and proteins. Their general health was excellent.

Treatment.

The six adult patients received 1 g. of griseofulvin, and the two children 0·5 g. of griseofulvin daily, divided into four equal doses. The treatment was continued for 70 to 78 days. The patients were divided in two groups of four, which as far as possible were of similar ages and sexes.

At the start of treatment, the patients of both groups had their hair cropped close. One group, comprising Cases 5 to 8, was treated by x-ray epilation with four-field irradiation (Nemenow, 1927 and Wagner, 1959), 50 kV., 25 mA, filter 1 mm. Al, F.S.D. 30 cm.

The other group was not submitted to irradiation, but had the hair cropped close once a week. No local treatment was given beyond washing and ordinary hospital tidying. During the period of treatment the patients wore light gauze caps fastened with tape.

Routine Examination.

The patients were examined clinically twice a week. Once a week the following examinations were made : weighing, chemical and microscopic urine analyses (including analysis for urobilin and bile pigment), haemoglobin, erythrocyte sedimentation rate, white blood cell count and ophthalmoscopy. At intervals of three weeks erythrocyte, thrombocyte, and differential counts, Takata-Ara and thymol turbidity tests, as well as serum urea determinations and serum protein analyses were performed.

Mycologic Examination.

Once a week the patients were inspected under Wood's light, and scrapings were taken for potash preparations and for six cultures on maltose-peptone-agar with penicillin and actidione. Each of the clinically suspicious regions was analysed, and the site of sampling was marked in a diagram, so that the site could be found again.

Results of Treatment.

After a week, the large crusts became detached along their borders, baring a thin, red, but dry epidermal surface, slightly depressed in relation to the surrounding skin. During the first few weeks after the detachment of the crusts, slight scaling and small, perifollicular infiltrations were seen. For practical reasons, the results are described in the following stages : (i) the last examination showing typical scutula, (ii) the last examination when scaling was still suspicious, (iii) the last examination revealing positive fungous cultures, and (iv) the last examination when potash preparations for fungi gave a positive result. *A priori*, a fairly long period of treatment was believed to be necessary, because scutula often displace the tissues to a depth of several millimetres, even if the deep layers of the epidermis are intact (Sabouraud, 1910). Table I shows that the scutula had disappeared after the 40th day, and that there was no suspicious scaling after the 54th day. Cultures were negative after the 33rd day, and the potash preparations after the 48th day. There was thus a fairly close time relationship between the detachment of scutula and negative culture, whereas scaling and fungi on direct microscopy were demonstrable one week later. Wood's light did not reveal changes that were not detectable in daylight. Mycological examination proved necessary during the period when typical scutula had disappeared, but suspicious scaling persisted. The results of the 26 tests made within this period are recorded in Table II. After scaling was no longer suspicious, another 35 mycological tests were performed, which

were all probably negative. In five of these, microscopy left some doubt, because it revealed short, multiseptate mycelial fragments with indistinct outlines. All the cultures however, were negative. Mycelia with ill-defined outlines may thus be regarded as insignificant.

As might be expected, the glabrous skin was cured more quickly than the scalp, the lesions being here more superficial. In the two patients with lesions of the smooth skin, culture was negative on the 5th and the 26th day respectively, while potash preparations were negative from the 12th and the 40th day.

In several cases, fungi were demonstrable by microscopy or culture from normal skin or pathological skin areas and nails which were not suspicious of favous. This is probably due to excessive amounts of scales being deposited on the skin where they adhere without causing actual infection, just as they may accumulate under the nails with scratching.

Two nails grew *Penicillinum brevicaule*, but this was not demonstrable after the 12th day of treatment. In one nail, *Trichophyton schoenleini* was found. After 57 days' treatment, the nail was removed. Fungi were cultured from the nail plate which had been removed, whereas the new-formed nail plate was clinically normal, and three cultures were negative. To judge from the results of cultures in this series of investigations, the treatment of favus of the nail can be effected in 8 weeks, provided infected nails are removed surgically. (This agrees with the statement of Degos, Rivalier and Lefort, 1959, concerning the hair.)

From the figures set out in Table I, x-ray epilation seems to be unnecessary.

Side Effects.

Mild subjective side effects were not recordable owing to confusion of languages. The patients were gay, apparently comfortable and gained on an average 3 kg. in weight.

Two patients developed a symmetrical eruption of the hands and feet on the 13th day, and one a similar eruption on the 23rd to 28th day, accompanied by an annular erythrosquamous eruption on the body. The exanthema subsided quickly under continued treatment.

All examinations of the fundus oculi were normal.

The results of the laboratory analyses before and after the treatment are shown in Table III. The changes being similar in all eight patients, only mean values for the whole group are given.

There was slight normochromic anaemia, which did not change after treatment with griseofulvin. The number of blood platelets was constant. The leucocyte values became slightly subnormal, but the ratio between polymorphonuclear cells and lymphocytes remained constant. It cannot be excluded that this shift was due to the griseofulvin. The E.S.R., which had been moderately

raised at the start of the treatment, dropped to almost normal values. Further, the distribution of the serum protein fractions altered somewhat, the originally slightly raised gamma globulin fraction becoming normal. This was probably due to changes in the patients' diet, from a low-vitamin diet rich in fats and proteins to a high-vitamin diet with a large carbohydrate content. Possibly, the changes in the protein level and the leucocytes were due to the eradication of various minor infections during the stay in hospital. Blood urea determinations and thymol turbidity tests gave values within the normal range both before and after the treatment.

The investigations revealed therefore, no signs of damage due to the griseofulvin, but three patients developed trichophytides, just as may occur during local treatment.

TABLE I.—*Progress Under Treatment with Griseofulvin.*

	Day of treatment.	Average.	Average for epilated cases.	Average for non-epilated cases.
Last observation of scutula	19–40	27	24	30
Last suspicion of scaling	47–54	49	48	50
Last positive culture	19–33	29	33	25
Last positive KOH-preparation	26–48	35	31	39

TABLE II.—*Results of Mycological Examination after Scutula had Subsided, but Scaling Persisted.*

KOH-preparation.	Culture.	Total.
++	+	3
−	+	1
+	−	6
Suspicious	−	2
−	−	14

TABLE III.—*Result of Laboratory Analyses (Means).*

	Before treatment.	After treatment.
Weight, kg.	46·1	49·8
Blood urea, mg. %	27·3	16·9
Thymol turbidity	0·0	0·09
Haemoglobin %	81	80·1
Erythrocytes/cu. mm.	4·0	3·8
Colour index	0·97	1·03
W.B.C./cu. mm.	5,700	3,900
Platelets/cu. mm.	285,000	289,000
E.S.R. mm./1 hr.	26·5	10·2
Total protein g. %	8·1	7·4
Albumin %	57·5	63·5
α_1 globulin %	3·4	3·4
α_2 ,, ,,	8·9	7·4
β ,, ,,	9·9	9·6
γ ,, ,,	20·3	15·9

Summary.

Eight cases of favus were cured clinically and mycologically by treatment for 70–78 days with 1 g. of griseofulvin daily in adults and 0·5 g. daily in children.

The treatment had no toxic side effects, but three patients developed trichophytides after 13–28 days' treatment. No pathological changes occurred in the fundus oculi, the blood picture or serum.

In most cases, cultures from the scalp became negative for fungi after the scutula had come off, and in all cases after the 33rd day. Scaling and microscopically visible fungous elements were not detectable after the 54th day. Favus disappeared earlier from the glabrous skin than from the scalp. As late as the 57th day, fungi were cultured from a nail removed surgically which had presented the clinical changes of favus.

Careful mycological examination is necessary as long as scaling is clinically suspicious, and treatment should be continued until cultures from such areas are negative.

Wood's light is of little aid as a supplement to clinical observation.

X-ray epilation had no influence on the result of treatment.

Cultures of *Penicillinum brevicaule* from clinically abnormal nails became negative during the treatment.

Griseofulvin was supplied by Leo Pharmaceutical Products as " Lamoryl ".

References.

Blank, H. and Roth, F. J. (1959) *Arch. Derm. Chicago*, **79**, 259.
Degos, R., Rivalier, E. and Lefort, P. (1959) *Bull. Soc. franç. Derm.* **66**, 281.
Esteves, J. and Neves, H. (1959) *Dermatologica, Basel*, **119**, 148.
Gentles, J. C. (1958) *Nature, Lond.*, **183**, 476.
Inman, P. (1954) *Brit. J. Derm.*, **66**, 409.
Lauder, J. M. and O'Sullivan, J. G. (1958) *Vet. Rec.*, **70**, 949.
Lomholt, G. (1959) *Ugeskr. Læg.*, **121**, 1383.
Nemenow, M. Y. (1927) *Urol. Cutan. Rev.*, **31**, 159.
Oxford, A. E., Raistrick, H. and Simonart, P. (1939) *Biochem. J.*, **33**, 240.
Sabouraud, R. (1910) *Les Teignes.* Paris : Masson.
Wagner, G. (1959) in *Handbuch der Haut-und Geschlechtskrankheiten, Ergänzungswerk* V/2. Berlin : Springer.
Williams, D. I., Marten, R. H. and Sarkany, J. (1958) *Lancet*, ii, 1212.

GRISEOFULVIN AND FAVUS.

A Report on Work in Progress.

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The astonishing promise of griseofulvin as an antimycotic agent has caused a considerable number of dermatologists to burst into print with enthusiastic preliminary reports on its apparent value in the treatment of the superficial mycoses (Williams *et al.*, 1958 and 1959; Blank and Roth, 1959; Latapi, 1959; Pardo-Costello *et al.*, 1959; Riehl, 1959*a* and *b*; Mitchell, 1959; Kirk and Ajello, 1959 and Cochrane and Tullett, 1959). Most of these reports, although interesting, have an unfortunate factor in common—the time spent in following up the patients seems to have been reduced to an unscientifically low period, and indeed some papers actually report cases which were still being treated at the time of writing. My paper reports work in progress on the treatment of favus with griseofulvin. It comprises the first fifty cases of a series, which at the time of writing amounts to more than 170 patients. In 38 patients, the shortest period of observation was three months from the cessation of treatment.

Favus is endemic in many parts of the Middle East and is one of the major Public Health problems, contributing almost 11% of the cases seen at the University Clinic of Dermatology in Tabriz (Pettit, 1960). In the past, attempts at epilation, either with x-rays or thallium acetate met with some success, but the large number of people who were not cured is shown by the considerable proportion of the population with extensive cicatricial alopecia. The disease usually dies out in the early twenties, although it is not uncommon to find a person of twenty or thirty years who still has a small amount of fungus in the hair. Most of the cases of favus presenting at the hospital were in people in the first two decades of life. In all cases the clinical diagnosis was confirmed by the demonstration of fluorescence in the hairs when examined under Wood's light and also by the recognition of the fungus microscopically. In view of the characteristic appearance of *Trichophyton schoenleini* under the microscope, it was not considered necessary to culture hair samples from all patients. This was done in the first twenty cases, but the practice was not continued.

Practical difficulties in this work were presented by the fact that unfortunately many of the local patients have not yet developed as much reliance on a hospital as those in Western countries and a number of people did not attend regularly for treatment. It had been hoped that each patient would attend weekly for treatment and observation, but a large number slipped (temporarily

or permanently) through our fingers. This number was reduced to a minimum by the enthusiastic help of the Health Visitors in the Tabriz Public Health Department whose detective ability, in a country where houses are not numbered, is second to none.

Research into a new treatment is always difficult and particularly so when at the start of the work neither the efficacy of the drug nor its dosage is known. For this reason it has been decided to give a " blow-by-blow " account of the work in the first few weeks. It was initially decided, on the advice of the Glaxo Laboratories whose munificence made this work possible, to treat all patients with four 250 mg. tablets daily, and the patients were seen weekly. At the end of the first week, there was no dramatic change, except that in the acute cases the scalp was a little less red, but at the end of the second week, those patients with scutula seemed definitely to show an improvement as the scaling and crusting were diminished. It was not until the third week of treatment that the clinical appearance of the non-fluorescent roots of the contaminated hairs gave reason to believe that the treatment was efficacious. The first few patients were treated for five weeks but it was soon realized that four weeks were enough and the patients were ordered to shave their heads at the end of the fourth week of treatment. By this time the non-contaminated portion of the hair is long enough to ensure almost certainly that the whole of the infected part of the hair is removed, even after the rather inadequate shaving that was often seen. One week after the shaving, the head was again examined for fluorescence. If any of the remaining hairs showed terminal fluorescence it was usually a simple matter to remove them manually or, if too many remained, to order a further shave in a few days' time. Children under five years were usually given only 125 mg. four times a day, and this routine would have continued if patient 12 had not failed to return after two weeks' treatment. This was a boy of seven years who, when first seen, had a few scutula and no obvious loss of hair, although about a quarter of the scalp was fluorescent. He had received four tablets a day for two weeks and when he returned to hospital five weeks after the start of his treatment and without having had any treatment for three weeks, it was seen that the fluorescence was growing out. When he was last seen, fourteen weeks after the end of treatment, he was cured. This experience indicated that a reduction of the dose was probably permissible, and from then on the dosage was 1 g. daily above the age of 12, 750 mg. from 7 to 12, and 500 mg. below the age of seven.

Table I summarizes the first 38 cases which were adequately followed for a period of at least three months after the end of the course. In this table the patients are placed in three grades of severity. The lowest grade was that type of patient who showed redness of the scalp, usually in a follicular distribution with some matting of hairs and no definite hair loss ; the next grade was that

of patients who showed loss of hair and more widespread redness with the presence of scutulae, in greater or lesser numbers. It is interesting to note that the emphasis placed on the diagnostic value of scutula is exaggerated in

TABLE I.—*Details of Cases Observed for at least Three Months after Completion of Treatment.*

Case No.	Age (years).	Severity.*	Dosages. No. of 250 mg. tablets.	Dosages. Duration (days).	Result.	Length of observation (weeks).
1	7½	++	4	35		22
7	10	++	4	35		20
9	13	+++	4	28		18
10	2½	++	2	28		18
11	6	+	4 2	28 7		19
12	7	+	4	14		14
15	5	+++	4	35		18
18	20	+++	4	35		19
19	12	+	4	28	Cured	19
20	5	++	4	28		18
23	10	++	3	28		16
24	12	++	2	28		15
25	5	+	2	28		15
27	5	+	2	28		16
29	12	+	3	21		18
32	7	++	3	28		20
33	12	+	4	28		15
41	12	+	4	28		14
42	3	+++	2	28		13
44	13	++	4	28	Relapsed	—
47	9	++	3	28	,,	—
50	7	+++	2	28		15
53	3	++	2	14	Cured	19
54	3	+	2	14		14
56	12	++	3	21		14
58	13	+++	2	14	Relapsed	—
59	4	++	2	28	Cured	14
60	2	+	2	14	? Relapsed	—
62	11	++	4	28	Relapsed	—
65	25	+++	4	28		16
66	1¼	+	2	21		16
67	6	+	2	28		14
68	7	+	2	28		14
71	6	+	2	28	Cured	13
73	2	++	2	28		13
74	13	+	2	28		13
75	5	+	2	28		13
76	9	+	2	28		13

*+ = redness, no definite loss of hair.
++ = more widespread redness, loss of hair, some scutula.
+++ = loss of hair over one-third of the head, atrophy and peripheral activity.

most Western textbooks and in Iran only about half the patients show these yellow crusts. The third grade was limited to those who had loss of hair over at least one-third of the head with atrophy in the bald patches and definite signs of activity at the periphery of the lesions. Most of these patients had extensive scutula formation among the roots of the remaining hairs. It will be seen that five of the 38 cases did not apparently derive the full benefit

which had been hoped for. It is interesting to examine these cases in greater detail.

Case 44.—A boy aged 13. When treatment was started he had widespread loss of hair with early cicatrization of about a quarter of the affected area and also considerable scaling, a number of scutula and many fluorescent hairs at the periphery of the bald area. The condition had been present for six years. He was given a full course of 1 g. daily for four weeks, and attended regularly. For fifteen weeks after the end of the course there was no sign of activity. He then suddenly produced a small scutulum and two fluorescent hairs. In spite of his denials about the presence of the disease in his brothers and sisters they were brought to hospital but were found to be free from infection. One week later he brought along his best friend who had severe favus. It could therefore be considered that this case was simply suffering from reinfection and that the original attack had been cured.

Case 47.—A girl aged 9. She had favus for a year before beginning treatment and showed a rather "moth-eaten" appearance on the scalp with patchy loss of hair and hairs with the lustreless dark grey appearance that sometimes indicates that they will be fluorescent. As she was only nine years old she was given 250 mg. thrice daily and the hair was shaved at the end of four weeks' treatment. Six weeks later, four fluorescent hairs were seen and manually epilated and a week later a further six were removed—all these showed the presence of fungus microscopically. A further nine weeks surveillance showed no further infection. At a later date her brother (case 78) was brought for treatment and so it is difficult to decide whether this was a matter of relapse or reinfection. In either case it is interesting to note that rapid recognition of the disease, associated with local epilation, may satisfactorily prevent the need for a further course of treatment.

Case 58.—A girl aged 12. In the present series this girl was one of the most severly affected and showed yellow crusts over the majority of the scalp with at least 50% loss of hair. She had failed to obtain a cure from two x-ray treatments. She was given 1 g. of griseofulvin daily and defaulted at the end of the second week because the crusts had nearly all come away and her mother thought she was better. We traced her three weeks later and she was told to shave the head, but this was inadequately done and had to be repeated a week later. Eight weeks after she had stopped treatment, the scalp showed several scutula which multiplied rapidly in the following few days. This was undoubtedly due to insufficient treatment. The rapid increase of scutula on the scalp indicates that within eight weeks there is total excretion of griseofulvin and long term protection is not given to the patient (cf. case 47 where protection lasted less than six weeks after a full course of treatment).

Case 60.—A boy aged 2. This little boy named Karib had a two months' history of crusting and redness in a follicular distribution. Hairs in each lesion showed the presence of fungus. He was given 250 mg. of griseofulvin twice a day and failed to return after fourteen days' treatment. Three months later he was found by the Health Visitors and on examination there was no fluorescence. At that time the Health Visitor also informed the department that there were twelve other children in the house, and instructions were given for them to attend. The child's mother returned four days later with a young child she said was Karib, who had acute favus with widespread fluorescence. It is not unknown for a parent to substitute one child for another in the hope of getting "two for the price of one" treatment, and I am unable to decide whether he was cured or not as the mother has not returned to hospital.

Case 62.—A girl aged 11. She finished a full course of 1 g. daily for four weeks and showed every sign of cure, but six weeks later three hairs were found to fluoresce. In spite of manual removal, increasing numbers of hairs became affected and a further

course of treatment was started which continues at the time of writing. Investis gation of the family showed that an older sister, aged 23 years, who used to dres- the child's hair, had a fungus infection of the right index-finger nail which, on culture, proved to be favus.

Of the five cases which have been marked down as failures, it can be seen that three can be explained as reinfections from the family or a friend, and a fourth (Case 60) was either in the same group or was cured. Only one can be attributed to underdosage. With this series in mind, and noting that all but one of the five " failures " returned voluntarily for further treatment when they realized that all was not well, it seems justifiable to add a further table (Table II). This includes a series of patients who attended for the course of treatment and only defaulted during the weeks of follow-up. It is probably true that the practical-minded Iranian saw no reason to continue weekly attendances when all seemed well.

TABLE II.—*Details of Cases Observed for less than Three Months.*

Case No.	Age (years).	Severity.*	Dosage. No. of 250 mg. tablets.	Dosage. Duration (days).	Condition when last seen.	Length of observation in weeks.
2	8	+	4	28	Satisfactory*.	2
8	6	+	4	35	,,	4
17	25	++	4	28	,,	3
31	5	+	2	28	,,	5
34	4½	++	2	28	Clear†	7
35	17	+++	4	28	Satisfactory	3
45	5	+	2	28	,,	5
52	7	+	2	14	Clear	7
57	7	++	2	14	,,	7
69	12	++	3	28	Satisfactory	3
70	7	+	2	28	Clear	6
72	7	++	2	28	,,	8

*+ = redness, no definite loss of hair.
++ = more widespread redness, loss of hair some scutula.
+++ = loss of hair over one-third of the head, atrophy and peripheral activity.
* i.e. fluorescence growing out.
† i.e. no fluorescence remained.

There has been considerable discussion about the possibility of untoward side effects, but in the 50 cases reported here (indeed in the whole of the 200 cases of favus or *Trichophyton tonsurans* infection which are under observation) only two cases are worthy of mention. Case 42, a child of three years with a severe infection of the scalp, developed papular urticaria during the second week of treatment. This disappeared before the end of the four-week course which was not interrupted and there seems to be no reason to regard this as more than a coincidence. Another child was brought to the hospital uncon- scious after taking only three tablets, but on admission to the children's depart- ment he was found to have a meningococcal meningitis from which he died. Again it seems highly unlikely that there was an aetiological connection.

It is considered that enough evidence is offered in this short paper to show beyond doubt that griseofulvin is the treatment of choice in favus. The risks inherent in treatment with thallium acetate have already caused it to be discarded in countries where radiotherapy is easily available, but in less fortunately endowed countries, thallium acetate is still used by many doctors, whose dislike of the treatment often causes them to use doses which fail to cause epilation. Irradiation is not easy to administer and the well-known ability of *T. schoenleini* to resist even this treatment quite frequently has proved to dermatologists who work in the endemic areas that neither treatment is perfect. In the present short series of cases only 10% of the patients needed any futher treatment, and there is no certain evidence that any patients who were adequately treated and managed to avoid contact with other cases failed to obtain a cure. It is obvious that the definitive dose of this drug is not yet known but further work is being carried out in this department and it is hoped that a further report will be offered which will show the results of a deeper study into this problem. At least we know that the " penicillin of the dermatomycoses " is as great a benefit to patients with favus as it is to other sufferers from ringworm.

References.

Blank, H. and Roth, F. J. (1959) *Arch. Derm., Chicago*, **79**, 259.
Cochrane, T. and Tullett, A. (1959) *Brit. med. J.*, **2**, 286.
Kirk, J. and Ajello, L. (1959) *Arch. Derm., Chicago*, **80**, 259.
Latapi, F. (1959) *Sem. med. Mex.*, **20**, 113.
Mitchell, J. (1959) *Irish J. med. Sci.*, **404**, 363.
Pardo-Castello, V. *et al.* (1959) *Bol. Soc. Cubana Derm. Sif.*, **16**, 1.
Pettit, J. H. S. (1960) *Brit. J. Derm.*, **72**, 000.
Riehl, G. (1959) *Wien Klin. Wschr.*, **71**, (12), 215.
——— (1959) *Hautarzt*, **10**, 136.
Williams, D. I., Marten, R. H. and Sarkany, I. (1958) *Lancet*, ii, 1212.
——— ——— ——— (1959) *Brit. J. Derm.*, **71**, 434.

INTERMITTENT TREATMENT OF TRICHOPHYTON RUBRUM INFECTIONS WITH GRISEOFULVIN.

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Numerous observers have confirmed that griseofulvin is of benefit in the treatment of *Trichophyton rubrum* infections (e.g., Blank *et al.* 1959; Barlow *et al.* 1959 and Williams *et al.* 1959). Despite the amount of work carried out, the smallest effective dose, the duration of treatment required and the relapse rate after clinical cure are still undetermined. The final results of treatment with griseofulvin in toe nail lesions, the possibility of drug resistance and the development of long-term toxic effects are also unknown. The aim of this paper is to elucidate some of these points and to present the results of treatment with intermittent doses of griseofulvin.

Investigation.

Fifteen patients with extensive and intractable *Trichophyton rubrum* infection were assessed. In every case skin and nail scrapings were taken for microscopic examination and culture on Sabouraud's glucose-peptone agar medium. Mycelia were found on microscopy in all patients and positive cultures were obtained in thirteen. The patients' ages ranged from 13 to 56 years; infection had been present for 8 months to 14 years. Eight patients complained of having had dry hands and feet for many years prior to infection.

The patients were divided into two groups. One group received continuous treatment with griseofulvin, 2 g. daily in divided doses; the other received intermittent treatment with griseofulvin, 2 g. daily in divided doses for two consecutive days in every seven. Griseofulvin has now been administered for 3 to 9 months. Eight patients have been treated by intermittent and seven by continuous dosage. Most are still receiving the drug. White cell counts were made before treatment and at increasing intervals.

Results.

All the patients have improved. Clinical cure was confirmed by the absence of mycelia on microscopic examination of scrapings from the previously affected areas.

Eleven patients complained of pruritus before treatment; in all of these it was dramatically relieved within the first three weeks of treatment, independent of the dosage used. Two patients complained of intermittent attacks of pruritus, which have not recurred since treatment was started. No significant difference in the rate of clinical improvement was noted between the two groups of patients. Response varied according to the sites involved.

(i) *Infection of smooth skin.*—The only patient in this group had lesions on the neck in addition to the palms, soles and nails. He received continuous treatment with griseofulvin and the lesions on the neck cleared in three weeks.

(ii) *Infection of palms and soles.*—Palms or soles were involved in all patients. They were clear of infection in 2 to 12 weeks and 3 to 16 weeks in the intermittent and continuous dosage groups respectively.

(iii) *Infection of finger and toe nails.*—Improvement of all involved nails was noted during treatment. There was some variation in the rate of regrowth of normal nail, but this was unrelated to the dosage schedule employed. As expected, finger nails cleared in 3 to 4 months in most cases. Toe nails, particularly the great toe nails, improved much more slowly. During the course of the trial 50% of involved finger nails and 15% of toe nails in the intermittent dosage group have cleared compared with 65% and 10% in the continuous group. The time required for clearance of infection obviosly depends upon the degree of nail involvement. One patient in whom both soles and five toe nails were mildly involved was clear in 10 weeks. Intermittent treatment with griseofulvin was stopped after 14 weeks, and he is still clear 20 weeks later.

(iv) *Nodular lesions.*—One patient had nodular lesions of the calf, similar to those described by Cremer (1953) and Wilson *et al.* (1954), in addition to involvment of both soles and all toe nails. She was treated continuously with griseofulvin and the nodular lesions disappeared in 8 weeks.

Side effects.

In no case did these necessitate withdrawal of the drug.

(i) *General.*—Several patients experienced mild headache. One patient developed acute urticaria which settled rapidly after treatment with antihistamines by mouth. It was thought to be unrelated to the treatment with griseofulvin which was not stopped. Another patient complained of anorexia, weakness and insomnia, but these passed off whilst treatment with the drug continued.

(ii) *Haematological.*—Two patients, one in either group, showed slight leucopoenia and lymphopoenia during treatment. In both cases, the count returned to normal over several months during the continued administration of the drug. Two patients, one in either group, had atypical lymphocytes in the peripheral blood on occasions. The patient on intermittent dosage had a normal white cell count ; the other had a count of 10,000 per cu. mm., and with 15% monocytes.

Discussion.

No series has previously been reported in which intermittent and continuous schedules of dosage with griseofulvin have been compared. Assessed by the

rate of improvement, the two schedules were found to be equally effective. Intermittent dose treatment is rational as its aim is to cause the deposition of layers of griseofulvin in newly forming keratin. There are insufficient cases in the series for statistical analysis ; griseofulvin was taken for different periods of time and the degrees of nail involvement varied from patient to patient. The results are, however, clinically impressive. The advantages of intermittent dosage are the smaller total amounts of drug taken with less danger of possible long-term toxic effects and the reduced cost of treatment with an expensive drug. The results agree with those of other workers (Blank *et al.* 1959 ; Barlow *et al.*, 1959 and Williams *et al.*, 1959). Speed of cure varied with the site of involvement, in the following order of increasing difficulty—smooth skin, palms and soles, finger nails and toe nails. On average, the duration of treatment required was for smooth skin 3 weeks, palms and soles 8 weeks, finger nails 16 weeks and toe nails probably well over a year, at the present rate of progress. Toe nails present the greatest difficulty and the most rapid method of treatment may prove to be surgical removal of the nails, unpleasant as it is, together with systemic administration of griseofulvin. It would seem wise to continue treatment for some time after clinical cure in order to reduce the possibility of re-infection of what may be abnormal keratin (Williams *et al.* 1959). Eight patients in this series complained of dry hands and feet for some years prior to infection.

Side effects were insignificant, and reports of these in the literature are few, considering the large numbers of patients who must by now have been treated with this drug. Whether long-term toxic effects occur, however, it is not yet known.

Summary.

Fifteen patients with *Trichophyton rubrum* infections were treated with griseofulvin by mouth. Eight received intermittent and seven continuous dosage.

There was no apparent difference in the response to treatment of the two groups.

Advantages of an intermittent dosage schedule of griseofulvin are that equal therapeutic results are achieved with a smaller quantity of this drug, the cost of treatment is less and the danger of possible long-term toxic effects is diminished.

References.

Blank, H. and Roth, F. J. (1959) *Arch. Derm., Chicago*, **79**, 259.
Barlow, A. J. E., Chattaway, F. W., Hargreaves, G. K. and La Touche, C. J. (1959) *Brit. med. J.*, ii, 1141.
Williams, D. I., Marten, R. H. and Sarkany, I. (1959) *Brit. J. Derm.*, **71**, 434.
Cremer, G. (1953) *Dermatologica, Basel*, **107**, 28.
Wilson, J. W., Plunkett, O. A. and Gregersen, A. (1954) *Arch. Derm. Syph. Chicago*, **69**, 258.

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TREATMENT OF NOCARDIAL MYCETOMA WITH SULPHAMETHOXYPYRIDAZINE.

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MYCETOMA may be caused by various species of *Nocardia*. It is a chronic suppurative granuloma of the subcutaneous tissues of the foot, characterized by progressive enlargement and deformity due to the presence of multiple deep abscesses which tend to break down and form sinuses. The discharge is a purulent material containing colonies of organisms or "granules". Nocardial mycetoma is widespread and is found most frequently in tropical and subtropical countries. However, it is thought to be uncommon in Thailand and there is only one Siamese case on record. Chamuni (1934) reported this case of nocardial mycetoma of 7 months' duration in a 37-year-old countrywoman. Following a small wound in her foot, a sinus developed and the discharge contained white granules. Culture was positive for *Nocardia madurae*. In our case, the organism was *Nocardia asteroides*.

We believe that nocardial mycetoma is not so rare as had been reported. In Thailand, most of the clinics for treatment of skin diseases are in Bangkok, the capital, while this disease is more common in the rural areas, among the farmers and gardeners. Many cases will most probably continue to be overlooked and misdiagnosed unless the disease is borne in mind.

Peters (1945) and Calero (1947) reported that sulphonamides may cure localized nocardial mycetoma. Sulphadiazine, sulphamerazine and "Triple Sulfas" (equal parts of sulphadiazine, sulphamethazine and sulphamerazine) showed a high degree of clinical effectiveness in some cases. However, the doses recommended were rather high and blood concentration levels ranged from 10 to 20 mg. per 100 ml. Consequently, several untoward renal and haematological complications were reported. Lamb *et al.* (1953) reported that "Triple Sulfhas" were not effective in his case, but that his patient responded very well to pregnenolone acetate.

Sulphamethoxypyridazine is a new sulphonamide with claims of low toxicity. It is readily absorbed from the gastrointestinal tract and is highly soluble in the urine with very slow urinary excretion and poor acetylization. High and long-lasting blood concentrations are attained within a short time with relatively low oral dosage. Sheth (1958) found from a study of blood levels

in adults with different dose schedules that by administering an initial dose of 2 g. sulphamethoxypyridazine, followed by 1 g. daily, the average level of pure sulphonamide in the blood ranged from 15 to 22 mg. after 2 hours, 19–26 mg. after 24 hours and 22–26 mg. after 120 hours. Vinnicombe (1958) studied the side effects of sulphamethoxypyridazine in 110 patients with non-specific urethritis who were given doses three times higher than the recommended dose of 1·5 g. per day. He found that only 10% of his cases had mild side effects, chiefly headache, which subsided within 24 hours after termination of treatment and there were no serious manifestations of drug toxicity or sensitivity ; de Castaneda (1957) similarly reported evidence of minor intolerance in 7 out of a series of 24 patients, in the form of nausea, headache, vomiting and rash. His dosage averaged 1·5 g. per day for adults. There were no renal or haematological complications.

Fig. 1.

Case Report.

A man aged 33, attended the O.P.D. of the Royal Thai Army Hospital, Bangkok, complaining of painless ulcers with sinus formation and discharge over the dorsum of the right foot for 10 years. He had never injured that foot. The lesion started with painless indurated nodules which ruptured spontaneously and discharged a serous exudate. Two years later, the nodules were excised. No medication was given. After six months, there were new sinuses over the affected area with serous discharge. A series of treatments then followed : UVR, arsenical preparations, penicillin and local applications, all of which were ineffective. Several more new painless indurated nodules with sinuses formed. The ankle and the dorsum of the right foot were swollen and made the patient limp.

On examination.—The patient appeared healthy, but limped. General examination was normal. The right ankle and dorsal surface of the right foot were swollen, moderately hard and comparatively bigger than the left foot. There were multiple indurated painless nodules with multiple sinuses (Fig. 1). The discharge was an oily, purulent material containing white-yellowish granules. There was no pain or tenderness on palpation.

Investigations.—The total blood and differential counts and E.S.R. were normal. Serologic examinations for syphilis were negative. Urine and stool examinations were normal. A roentgenogram of the chest showed normal lung fields, and one of the right foot showed no destruction of bone.

Pus from draining sinuses contained numerous white pinpoint granules. On microscopic examination, the granules appeared to be irregular masses of delicate filaments without clubs. Stained smears of crushed granules showed delicate short-branching filaments which were gram positive and partially acid fast. Aerobic cultures of pus on brain-heart infusion blood agar at 37° C. and on Sabouraud's dextrose agar at room temperature yielded small round raised and whitish colonies with a slight musty odour after 72 hours. Stained smears from these colonies showed delicate partially acid-fast mycelium. Culture on Czapek's solution agar at room temperature appeared ochraceous yellow on the surface with patches of currant red on the reverse. Slight short white aerial mycelium appeared on the surface of the old culture. Litmus milk was neither acid nor coagulated. Gelatin was not liquefied.

A saline suspension of a three-week-old culture on Sabourand dextrose agar injected intraperitoneally into a guinea-pig produced a large abscess of the right ovary adhering to the abdominal wall and also small abscesses in the omentum after fourteen days.

The organism was recovered from the ovarian abscess. Histological sections of the omentum revealed numerous micro-abscesses with granules of actinomycotic type. Some of these showed clubs. The cellular reaction was of suppurative type, consisting of a mixture of polymorphonuclears and lymphocytes. Only few large mononuclear cells were seen. No giant cells were found. The final mycological diagnosis of the fungus was *Nocardia asteroides* (Eppinger) Blanchard, 1896.

Histological examination of a biopsy specimen from the patient's skin showed that the epidermis was acanthotic. In the dermis, there was an increase in capillaries and a diffuse infiltration of inflammatory cells, chiefly neutrophils. In some places there were micro-abscesses with granules at the centre.

Treatment.—Treatment with penicillin 1,000,000 I.U. daily for 10 days, streptomycin 1 g. daily for 15 days and local applications was ineffective. Sulphafurazole was tried in big doses to obtain a high blood concentration level. A daily dose of 5 g. was given orally for 5 days without complication. Dosage was then raised to 6 g. daily for 20 days. However, there was no improvement. The discharge still contained white granules and new lesions developed.

An initial dose of 2 g. sulphamethoxypyridazine was then given orally, followed by 1·5 g. daily. Ten days after this treatment was instituted, there was a sharp decrease of the purulent discharge and the white granules greatly diminished in number. The microscopic picture of the granules was not as well formed as before. After this time, no new lesions appeared. By the end of three weeks, the sinuses narrowed and there was almost no discharge and no granules were found. After two months' treatment, the sinus openings healed. The swelling of the right ankle was reduced, most of the indurated nodules showed almost complete flattening, and the entire affected area was softer.

The patient was then transferred to some post and did not take the medicine for one month. Treatment was then resumed. During his absence, no new lesions formed. Dosage was started again at 1·5 g. daily and continued for another month

and a half. During the treatment, routine blood and urinary microscopic examinations were made at weekly intervals. The results were within normal limits. No significant side effects occurred during these two periods of treatment. The patient was still in the best of health.

Discussion.

Sulphonamides have been found effective in certain cases of mycetoma due to *Nocardia*. High doses are recommended to obtain a high blood sulphonamide level which has to be kept up for 3–4 months after apparent cure to ensure complete recovery. Haematological and urinary complications are often associated with other side effects.

There is no doubt that sulphamethoxypyridazine gave an excellent therapeutic result in this patient. The dosage used was remarkably lower than that of other sulphonamides. A dose of 1·5 g. was given daily for 4 months without any complications. Healing and narrowing of the sinus tracts, and reduction of the discharge and granules were noted in two weeks. Within six weeks, all the sinuses closed and there was no discharge. No relapse has been noted.

Sulphamethoxypyridazine is the drug of choice and is preferred to pregnenolone acetate and the sulphonamides which have previously been tried. It is more economical than pregnenolone acetate for long-term therapy. It is easier to administer than pregnenolone acetate as it is taken orally. The dose is only 1·5 g. daily, so there is less tendency towards gastrointestinal disturbances. No haematological or urinary complications or other side effects were encountered.

Summary.

A case of nocardial mycetoma caused by *Nocardia asteroides* is reported for the first time from Thailand. It was treated successfully with sulphamethoxypyridazine. The dose was 1·5 g. daily for 4 months. There were no untoward reactions. No relapse has been observed.

The sulphamethoxypyridazine used in this study was supplied by Dr. Yukon Hemachudha, Medical Director, F. E. Zuellig (Bangkok) Ltd., agents for Lederle Laboratories, Cyanamid International, New York, U.S.A.

References.

Calero, C. (1947) *Arch. Derm. Syph., Chicago*, **55**, 761.
Castaneda, J. de (1957) Preliminary report to Lederle Laboratories.
Chamuni, A. (1934) *Med. J., Bangkok*, **17**, 641.
Lamb, J. H., Kelly, F. C., Shackelford, P. O., Rebell, G. and Koons, R. C. (1953) *Arch. Derm. Syph., Chicago*, **67**, 141.
Peters, J. T. (1945) *Amer. J. trop. Med.*, **25**, 363.
Sheth, U. K., Kulkarni, B. S. and Kamath, P. G. (1958) *Antibiot. Med.*, **5**, 604.
Vinnicombe, J. (1958) *Ibid.*, **5**, 474.

THE TREATMENT OF CUTANEOUS TUBERCULOSIS WITH DIETHYL DITHIOL*ISO*PHTHALATE.

A Preliminary Report.

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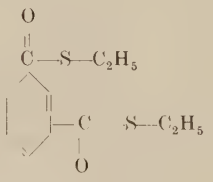
In 1950, del Pianto claimed that a mixture of certain thiol compounds prevented the development of tuberculosis in infected guinea-pigs and in 1956 Davies *et al.* traced the active principle to ethyl mercaptan and compounds capable of forming it. This property was limited to the ethyl homologue and was evident almost solely *in vivo*. They concluded that a metabolite of ethyl mercaptan was the ultimate active agent and suggested thiol esters as the most useful group of compounds for the treatment of human disease.

Davis and Driver (1957) chose diethyl dithiol*iso*phthalate (ETIP, Etisul, I.C.I.) as the most promising for therapeutic use. It had an antituberculous effect in mice comparable to that of isonicotinic acid hydrazide and streptomycin and was most effective when injected subcutaneously or applied to the skin. Its chemical formula is :



Davey and Hogerzeil (1959) conducted a clinical trial in cases of leprosy and found that if inunction of an extensive area of the body was carried out using 3–6 ml. twice weekly, the effect in the first two or three months of treatment was variable, but in some cases very marked indeed. In a more recent communication Davey (1959) has shown that the drug has a speedy action on the staining qualities of lepra bacilli and for this and other reasons it is likely that its action is more bacteriocidal than bacteriostatic.

Davies and Driver (1958) demonstrated the marked inhibitory action of ethyl mercaptan on intracellular tubercle bacilli, using a modification of Suter's method and a similar inhibitory effect was found using human monocytes from a case of monocytic leukaemia. This evidently explains why the previous authors found that the drug had little effect on the bacillus *in vitro* and suggested

1

2

3

4

Fig. 1.—Case 1 before treatment (19.vi.59).

Fig. 2.—Case 1 after treatment (15.ix.59).

Fig. 3.—Case 2 before inunction of right shoulder, 10 weeks after INH was discontinued (21.vii.59).

Fig. 4.—Case 2 after inunction of right shoulder (15.ix.59).

to us that as tubercle bacilli are found intracellularly in diseased tissue, local inunction of the drug in lupus vulgaris, for example, might produce favourable results. It appeared quite likely that ETIP would be broken down to ethyl mercaptan within cells containing bacilli, in addition, perhaps, to its liberation elsewhere in the body.

We therefore decided to test the effect of this substance in cases of tuberculosis of the skin when used by inunction and this preliminary communication reports the early results. It is hoped to publish a more comprehensive account of the clinical effects of this drug later.

Case Reports.

The cases so far treated fall into three groups.

(i) Two patients who had had little or no treatment.

Case 1.—A woman aged 41 years with untreated lupus vulgaris of the right temple of 8 years' duration (Fig. 1). ETIP (68% in magnesium stearate) was applied by inunction to the affected area and the surrounding skin for ten minutes daily over a period of five weeks, with very marked reduction in the colour and definition of the lesions. The clinical improvement in this patient was striking (Fig. 2). A great many of the nodules have disappeared.

Case 2.—A man aged 75 years with extensive lupus vulgaris of the face, neck, chest and back of 60 years' duration. Although he had received some local treatment of the face many years ago, ninety per cent. of the affected area had never been touched. He received isonicotinic acid hydrazide 100 mg. thrice daily for 5 weeks immediately prior to the present trial. ETIP was applied by inunction over a wide area of the right side of the back daily for two months (both sides of the back were almost symmetrically affected). The colour of all the nodules has now faded and oedematous areas on the face have subsided. The treated area on the right side showed no greater improvement than the left, but recent inunction of the right shoulder where the lesions were tumid has now led to considerable local improvement (Figs. 3 and 4).

(ii) Two patients who had in the past received prolonged courses of treatment by cauterization, radiotherapy, Kromayer lamp, calciferol and isonicotinic acid hydrazide, but who still presented active nodules enclosed in scar tissue.

Cases 3 *and* 4.—A man aged 53 and a woman aged 55, with lupus vulgaris of the face, who had received continuous treatment including radiotherapy for over 25 years. These were treated by local inunction of ETIP into the residual nodules in the scar tissue. Clinically, it was considered that improvement had occurred after three months, but photographic records do not afford definite confirmation.

(iii) *Case* 5.—A man aged 54 with scrofuloderma of the right leg of 25 years' duration, which had been treated for many years with resulting fibrosis. He was given inunctions of ETIP to the affected area for two months. Considerable reduction of oedema and of the granuloma was seen both clinically and in photographs. Treatment had to be discontinued, however, owing to an eczematous reaction to the ointment. A patch test with ETIP confirmed that this was due to contact sensitization.

The garlic-like smell of ethyl mercaptan in the breath (Davey and Hogerzeil, 1959) was not noticeable in the patients treated by inunction of small areas and only slightly in the one in which extensive areas were treated. A complaint was made of an unpleasant smell from the contaminated bed linen, possibly due to the perfume which had been incorporated in the preparation.

Comment.

This preliminary report is made to indicate the possibilities of a new percutaneous antituberculous remedy. Our experience suggests that it is most effective in cases of lupus vulgaris with the minimum of scarring. Rapid improvement after inunction of comparatively small quantities of ETIP into the lesion in Case 1 suggests that if the effect is due to the release of ethyl mercaptan, this must take place locally. An effect comparable with that seen in leprosy, where extensive inunction is followed by improvement of lesions remote from the site of application, is shown in Case 2, but local inunction may have enhanced the effect in the lesions in the area of application.

Cases 3 and 4, in which tuberculous nodules were embedded in scar tissue possibly due to previous radiotherapy, showed little or no response. In such cases absorption may be inadequate. Treatment is being continued in the hope that they will eventually improve.

Contact sensitization by ETIP was noted in one patient.

In the treatment of leprosy, Davey (1959) found ETIP valuable in combination with diaminodiphenyl sulphone. It seems likely that a similar combination of ETIP with isonicotinic acid hydrazide would offer a valuable adjunct to the chemotherapy of cutaneous tuberculosis.

We are grateful to Dr. J. M. Mungavin and the Pharmaceutical Division of I.C.I. Ltd., Wilmslow, Cheshire, for the supplies of ETIP (Etisul) and for their assistance in meeting the cost of the colour prints.

References.

Davey, T. F. (1959) *Leprosy Rev.*, **30**, 141.
——— and Hogerzeil, L. M. (1959) *Ibid.*, **30**, 61.
Davies, G. E. and Driver, G. W. (1957) *Brit. J. Pharmacol.*, **12**, 434.
——— ——— (1958) *Nature, Lond.*, **182**, 664.
——— ——— Hoggarth, E., Martin, A. R., Paige, M. F. C., Rose, F. L. and Wilson, B. R (1956) *Brit. J. Pharmacol.*, **11**, 351.
Del Pianto, E. (1950) *Ric. sci.*, **20**, 83.

TRANSVAAL DERMATOLOGICAL SOCIETY.

Johannesburg, 28 March,1959.

Epidermolysis Bullosa Resembling Juvenile Dermatitis Herpetiformis.—Dr. C. M. Ross.

A boy aged 8 years. The rash has been present since birth when there was a widespread bullous eruption ; impetiginization followed. The palms and soles were very hyperkeratotic; the mucosae were not involved. Histologically the bullae were intra-epidermal; there was no acantholysis.

Treatment with Dapsone 0·1 g. t.i.d. and terramycin ointment produced substantial improvement in both blistering and hyperkeratosis, but haemolytic anaemia occurred. The case is shown because of its obvious similarity to the 4 patients reported under this diagnosis by Drs. Dowling and Meara (*Brit. J. Derm.*, 1954, **66**, 139).

Note.—Dr. Dowling agreed with the diagnosis. A second course of Dapsone was less effective; at Dr. Dowling's suggestion Lederkyn 0·5 g. b.d. was given, with improvement.

Persistent Kerion-like Eczematous Dermatitis Progressing to Mycosis Fungoides.—Dr. H. Klevansky.

A man aged 49, was first seen two years ago with persistent kerion-like lesions on the scalp. These lesions did not respond to any of the broad-spectrum antibiotics, and numerous examinations for fungi were negative. For one year the appearance was identical with the condition described by Finn and Main (*Brit. J. Derm.*, 1956, **68**, 369).

During the last year some of these lesions have healed spontaneously leaving patches of alopecia, but he developed tumour-like plaques over the neck and on the lower lip. Histological examination showed a non-specific inflammatory infiltrate extending deep into the subcutaneous tissue, and plasma cells, lymphocytes, eosinophils and reticulum cells.

He has had Prednisone 60 mg. daily for several weeks without any benefit though the eczematous lesions on the face are kept under control with Fludrocortone ointment. He has had 300 r of x-rays to one area on the face without any response. General examination showed no abnormalities, blood count is normal, skiagram of lungs n.a.d.; liver and spleen are not palpable. Though the clinical diagnosis was considered to be mycosis fungoides, the unusual features were the localization to the face and neck and the persistent kerion-like lesions of the scalp which healed spontaneously leaving patches of alopecia.

Note 16.vi.59: This patient was admitted to hospital and has responded fairly well to larger doses of x-ray therapy.

He has now developed infiltrated plaques on the body.

Lipoid Proteinosis.—Dr. H. Klevansky.

A girl aged 7 years. One of 3 children with a history of a rash on arms and forearms from the age of 10 months. The mother has observed that the rash is always aggravated by sunlight and has gradually become worse during the last few years. A brother and sister show no evidence of skin disease.

The skin on the back of both hands, knees and elbows is erythematous and thickened, with a doughy feel. The transition from normal to affected skin is

indefinite. The face looks pock-marked; some of the scars are linear and evidently produced by scratching. General and laboratory examinations revealed no abnormality. Stool and urine negative for porphyrin. Histological examination confirmed the diagnosis.

Jessner's Lymphocytic Infiltrate.—Dr. M. Chitters.

A man aged 54. Onset 20 years ago of dusky red maculo-papular lesions on the forehead and cheeks, predominantly on the left. Cleared for a period of 12 years after 2 injections of bismuth. For the past 2 years the rash has come and gone. The effect of Chloroquine is uncertain but the rash clears promptly with corticosteroids, only to recur when medication is stopped. There is no apparent relation to sunlight exposure; the patient believes that emotional factors aggravate.

Histology.—Dense lymphocytic aggregates are present in the upper two-thirds of the corium, partly grouped around the blood vessels. The epidermis, vessels and adnexae are normal.

Generalized Trichophytosis and Buccal Moniliasis.—Dr. I. Gluckman.

Male aged 40. The condition began 3 years ago as tinea cruris and has spread to involve the face and large areas of the body and limbs. The lesions are erythematosquamous and considerably infiltrated in parts. The palms and soles are grossly hyperkeratotic and fissured. Typical thrush lesions are present in the mouth. Repeated skin scrapings showed fungal mycelium and on one occasion *Trichophyton concentricum* was grown. Swabs from the mouth showed *Candida albicans*. Biopsy showed a superficial dermatitis with abundant fungal elements in the horny tissue.

Note.—Dr. Loewenthal suggested that griseofulvin should be used. Rapid clearing of the skin lesions occurred with a dosage of 2 g. daily, subsequently reduced to 0·5 g. daily. After 3 months, the face, hands and feet are clear; a few scaly plaques are still present on the trunk. No change is seen in the buccal lesions.

Genodermatosis.—Dr. L. J. A. Loewenthal.

A woman aged 27. The skin complaint has been present since birth and becomes worse in summer. Itching is very severe around the genitals.

Family history.—Parents were brother and sister. Each has subsequently married and had numerous children; patient states none of her half-brothers or sisters are affected.

Clinical features.—The eruption affects the trunk and limbs and consists of circinate plaques, with peripheral extension and central clearing; a figurate outline is produced by coalescence. Bullae and crusts have been seen at the edges of lesions. Transient white patches have been present on the gums, above the upper incisors. External strabismus.

Histology.—Patchy thickening of the granular layer. Slight acanthosis. Moderate perivascular lympho-histiocytic infiltrate in upper corium.

Comment.—The appearances, with the exception of the bullae, bear a resemblance to ichthyosis linearis circumflexa (Comel, cited by Frank *Hautarzt*, 1956, **7**, 421). It is possible that this is identical with the *Génodermatose en cocarde* of Degos (Bazex and Dupré, *Ann. Derm. Syph., Paris*, 1956, **83**, 612). In both the above, improvement was noted in summer.

Dermo-hypodermite with Atrophy and Hypertrichosis.—Dr. L. J. A. Loewenthal.

A girl aged 17. History: Lumps have appeared in an area of the left leg for 8 years. They feel hot but are not tender unless knocked. They do not appear in precisely the same spot but anywhere in an area comprising the middle third of the

anterior and medial aspects of the leg. The patient notices that a shallow depression follows recovery of the lesions and states that hair growth is more noticeable in these areas.

The biopsy had been taken previously and barely reaches the hypoderm. At the lower edge there is a portion of cellular infiltrate, including a few giant cells.

Comment.—This case recalls that of Cerutti and Montagnana (*Hautarzt*, 1959, **10**, 33), who quote the two previous cases (but without hypertrichosis) of Gougerot and Bouvier; in all three the onset was in females before puberty.

Trophopathia Pedis Myelodysplastica (Sporadic Neurogenic Acro-osteolysis, Acropathie Ulcero-mutilante).—Dr. J. Cowley.

African man aged 24. Approximately 6 years ago he developed pains in both feet with subsequent swelling. One year later he noticed that his 5th right toe was slowly disappearing. He developed ulcerations on his soles and plantar surfaces of his toes; these ulcerations would partially heal with hospitalization and treatment but would recur on returning to his home.

The 5th right toe completely disappeared leaving ulceration and scarring at the base. The same process was occurring in the 5th left toe and the terminal phalanges of the 2nd right toe and big toe of the left foot were commencing to ulcerate and shorten. There were 3 large ulcers at the base of the toes on the left sole and 2 on the right sole. Superficial sensibility of both feet was affected but no definite pattern of sensory change could be mapped out.

Numerous blood chemistry tests were normal. The skiagrams were read by Dr. Eric Samuel, now senior radiologist at Edinburgh University, who pronounced that the plates were those of trophopathia pedis myelodysplastica and not those of the osseous changes that occur in neural leprosy.

Comment.—The case was presented on account of its rarity as well as on account of the very close similarity to the clinical picture as seen in leprosy. In point of fact, the case had been referred to a leprosarium and was diagnosed as a case of burnt out leprosy. I know of 3 other cases that have been diagnosed as osteolysis of the feet due to malnutrition. The condition has to be differentiated from syringomyelia, tabes dorsalis, spinal cord tumours, chronic osteomyelitis, tuberculous osteolysis, etc.

References.

Barnetson, J. (1950) *Acta radiol.*, **34**, 47.
Barre, J. A. (1945) *Rév. neurol.*, **77**, 211.
Giaccai, L. (1952) *Acta radiol.* **38**, 2.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

8 October 1959.

Dermatomyositis.—Dr. A. Girdwood Fergusson.

A man aged 42 whose present condition started in 1957 with pain in the shoulders and hips and at the same time a rash on the face, neck and arms. He had weakness, pain and limitation of movement of the arms and legs. The pain and weakness increased with activity. When the rash developed on his face, there was also swelling, particularly around the eyes. He was admitted to another hospital in April 1957, for investigation and treatment. Many investigations were carried out between

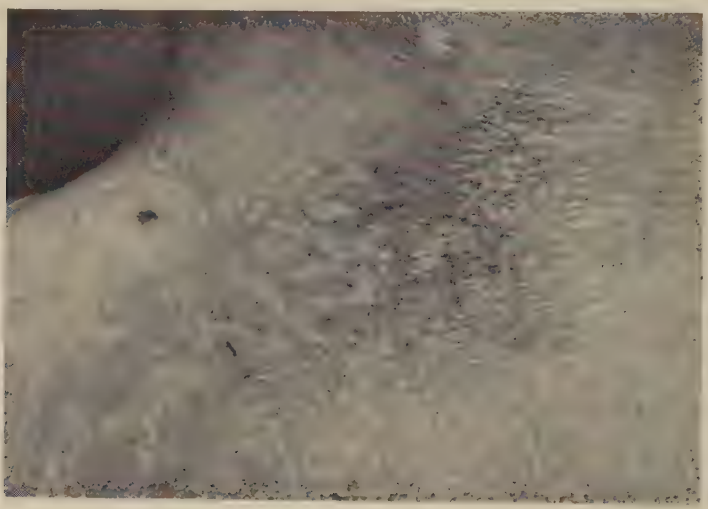


Fig. 1.

then and June 1958, during three admissions to hospital and many diagnoses were suggested. These included systemic lupus erythematosus, polyarteritis nodosa, pophyria cutanea tarda, scapulo-humeral type of muscular atrophy, and dermatomyositis. He was treated with ACTH and prednisolone in varying doses with partial but temporary response.

When admitted to the Department of Dermatology, Stobhill General Hospital in July 1958 he was found to have weakness of the arms and legs, more on the right side, with wasting of the muscles of the shoulder girdle (trapezius and triceps) and right hypothenar muscles. His skin showed a diffuse, dusky erythema and oedema of the face, particularly around the eyes. An eruption was noticed on the neck and there was some degree of patchy erythema of the hands. On the back of the neck and shoulders the eruption had the clinical features of poikiloderma atrophicans vasculare (Jacobi) (Fig. 1).

Investigation.—Skiagram of chest N.A.D. E.C.G. normal record. Haemoglobin—white blood count and red blood count normal. E.S.R. has varied between 5 and 6 mm. Blood urea normal. Blood culture negative. Serum electrolytes normal.

Serum calcium normal. C.S.F. normal. W.R. and Kahn negative. Urinary creatine and creatinine—these have varied on numerous occasions from creatine 70 mg. to 930 mg., and creatinine 450 mg. to 980 mg. L.E. cells have never been found. Plasma proteins show a reversal of AG. ratio. Liver function tests have been within normal limites. No abnormal porphyrins were found in the urine or stool. Glucose tolerance test normal. Serum G–O transaminase 30 units. Muscle reactions in July 1958, gave a weak response to faradism in the upper arms and gluteal muscles. The hamstring muscles showed weakness of the semitendinosus and semimembranosus, and in general the reaction on the left side was more responsive than on the right.

Histology.—Previous skin biopsies have revealed a non-specific picture and two previous muscle biopsies were reported as follows:

29 *June* 1957: There is infiltration of the fatty tissue and perivascular tissue with lymphocytes, histiocytes, and plasma cells. No necrosis of vessels. Mild degeneration in muscles. No diagnosis can be made as features are not characteristic of any one disease. Primary lesion appears to be a degeneration and inflammation of muscle. Periarteritis nodosa cannot be excluded.

5 *December*: 1957 Infiltration by lymphocytes, histiocytes, and plasma cells of fatty tissue and between muscle bundles. Muscle infiltration is greater than in the previous biopsy. Perivascular infiltrate is present. No necrotizing angiitis. There are degenerative changes in the muscle. Consistent with although not diagnostic of lupus erythematosus.

7 *October* 1959: Some changes in muscle suggest lupus erythematosus rather than dermatomyositis. (Dr. J. A. Milne.)

Progress and Treatment.—Since June 1958 the condition has gradually improved with a considerable return of muscle power. In November 1958, he had an attack of herpes zoster which appears to have been unconnected with his present condition. Treatment has consisted of chloroquine diphosphate, 250 mg. b.d., from 11 December 1958 to 11 November 1959.

Dermatomyositis.—Dr. A. Girdwood Fergusson.

A man aged 55 was first seen on 1 November 1959 with a history that in May 1959, he developed redness and itching of his hands and face associated with stiffness and pains in his shoulders and thighs. He found he was unable to lift his arms and his thighs felt tired after walking. His limbs became stiff after sitting.

Previous history.—In May 1957 he had a left upper lobectomy for a bronchial neoplasm. He has been attending a chest clinic at regular intervals since and his chest condition is satisfactory.

Examination.—There is a dusky erythema of the face and forehead, extending on to the scalp and upper chest, and an erythematous papular eruption on the backs of both hands and elbows. The shoulder girdle shows no diminution in movement but possibly slight wasting of some of the shoulder muscles. There is some pain on full flexion and adduction of the right hip and there is a very mild degree of quadriceps wasting. General examination reveals no abnormality.

Investigation.—Haemoglobin and white blood cells—within normal limits. No L.E. cells detected on two occasions. Skiagrams of chest and lumbar spine revealed no abnormality. Serum proteins 7·8 g.%; albumin 4·3 g.%; globulin 3·5 g.%. The electrophoretic pattern shows a moderate increase in α-globulins. Serum G–O Transaminase—8 Cabaud units. Fasting blood sugar 72 mg.%. 17-hydroxycorticoid content of 24-hour urine specimen 8·4 mg. Serum cholesterol 121 mg.%; chloride 99 meq. per litre; sodium 134 meq. per litre; potassium 4·6 meq. per litre. Urinary creatinine 1·07 g. in 24 hours. Urinary creatine 154 mg. Serum creatinine 0·7 mg.%. E.C.G. showed a normal record.

Histology.—(9 September 1959): Sections show no significant changes in the epidermis. There is a striking oedema of the entire corium, the collagen fibres being

splayed out by oedema fluid. There is patchy perivascular lymphocytic infiltrate. The appearances though by no means diagnostic are those seen in the skin in dermatomyositis. Muscle biopsy would be advisable.

(23 November 1959): Sections from the muscle submitted show foci of inflammatory change with interruption of muscle bundles. The appearances are those seen in dermatomyositis. (Dr. J. A. Milne.)

Parapsoriasis Lichenoides (Brocq) with Allergic Vasculitis (? Polyarteritis Nodosa).—Dr. A. Girdwood Fergusson.

A man aged 21 who three years ago developed a widespread, asymptomatic eruption which persisted despite various local applications.

Previous history.—General health good. He served in Egypt with the Forces, and returned two years ago being discharged with a disability pension for his skin complaint.

Family history.—*Nil* of note.

Examination.—There is a generalized blotchy erythema with slight scaling and crusting (Fig. 1).

Investigation.—Skiagrams of chest and thoracic and lumbar spine—no abnormality. E.C.G. normal record. Serum urea 23 mg.%; chloride 107, sodium 144, potassium 4·8 meq. per litre; proteins 6·5 g.%; albumin 3·7,g lobulin 2·8 g.%. Electrophoretic pattern normal. 17-hydroxycorticoid content of 24-hour specimen of urine (2640 ml.) —7·8 mg. falling to 0·8 mg. and 0·4 mg. following the exhibition of triamcinolone and methylprednisolone respectively. Urine—specific gravity 1020, reaction acid, no albumin, sugar, etc. W.R. negative. Haemaglobin 15·5 g./100 ml.; W.B.C. 6500. Film normal. Platelets 157,000 per cu. ml. Fasting blood sugar 77 mg.%. Stool examination (15 December 1959) revealed no parasites or ova.

Histology.—(18 March 1959): Skin sections show the histological features of an acute allergic vasculitis (? polyarteritis nodosa).

(21 August 1959): Marked perivascular lymphocytic infiltration although no acute vascular lesions are seen. (Dr. J. A. Milne.)

Progress and treatment.—Courses of steroid therapy were given on two occasions, 2 April 1959 to 19 May 1959 and commencing 27 August 1959. During the intervening three months the eruption recurred and it is re-appearing as the dose is reduced. Oral triamcinolone and methylprednisolone have both been found palliative.

Comment.—This may be either parapsoriasis with concomitant " allergic vascular disease ", or one of very unusual polyarteritis nodosa (without any evident nodal lesions) of the purely cutaneous type.

The following cases were also shown:

Prurigo Nodularis.—Dr. A. Girdwood Fergusson.

Dermatitis Herpetiformis (Pemphigoid Type).—Dr. J. C. P. Logan.

Sarcoid (Darier-Roussy).—Dr. J. C. P. Logan.

Chronic Arsenical Poisoning with Progressive Squamous Epithelioma.—Dr. J. C. P. Logan.

Mycosis Fungoides.—Dr. J. C. P. Logan.

Pre-mycotic Stage of Mycosis Fungoides. –Dr. J. C. P. Logan.

Case for Diagnosis.—Dr. P. W. Grant.

Scleroderma.—Dr. P. W. Grant.

Woolly-Hair Naevus (Wise) and Persistent Pupillary Membrane.—Dr. P. W. Grant.

Naevus Verrucosus.—Dr. P. R. Derblay for Dr. A. Girdwood Fergusson.

Favus (two cases).—Dr. P. R. Derblay for Dr. A. Girdwood Fergusson.

CORRESPONDENCE

The Editor, 'The British Journal of Dermatology',
85 Harley Street, London, W.1.

SIR,—Dr. R. H. Marten's contribution (*Brit. J. Derm.*, **71**, 422) strongly supports the belief that candida infection in the nail fold is derived from the bowel or mouth where it is commonly present as a saprophyte. It was his work, in conjunction with earlier publications on this subject, which suggested to me that the high incidence, statistically significant, of the primary lesion on the right middle finger fold (*Brit. J. Derm.*, **71**, 6) was the result of repeated exposure to contamination by micro-organisms from the bowel after defaecation. In children who suck their fingers or thumbs the obvious source would appear to be the mouth, but in adults the bowel is more likely.

Further evidence of the faecal origin of nail fold infection with candida has come to me by chance in the shape of a pustular folliculitis on the right middle finger of a medical colleague. The *Candida albicans* which grew from the pus in *heavy* and *pure* cultures was in his case almost certainly culled from one of his patients, because he used this finger—protected by only a short rubber finger stall—for rectal examinations ; and the part of of the finger affected was just proximal to, and therefore outside, the edge of the finger stall.

The somewhat unusual spectacle of *C. albicans* producing follicular pustules on the open skin of an otherwise healthy subject makes me wonder whether I have in the past given candida its due as a parasite. I have seen other medical colleagues with similar recurrent follicular pyodermata of the fingers which I dismissed as staphylococcal folliculitis, whereas they may well have been candida infections acquired from the same place and in the same way. If so it would explain the failure of local antibiotics to do them any good.

Yours etc.,

Cambridge. C. HOWARD WHITTLE.

CHRONIC PARONYCHIA.

SIR,—The author of this excellent paper (*Brit. J. Derm.*, **71**, 12) is to be congratulated on his painstaking analysis of cultures in this common clinical problem, on which many conflicting views have recently been expressed.

A minor criticism is the title. " Paronychia " refers to an acute inflammation or whitlow beside the nail, which could theoretically be at the free border or finger tip. " Perionychia " would seem preferable, as this indicates an inflammatory process around the nail fold.

I should like to draw attention to a varnish called Onychophytex containing a boro-tannic complex, which I have been using for nearly a year. If painted around the nail fold twice daily to form a seal, no further infection can enter, and the patient is not unduly handicapped. My results have been most gratifying. If there is associated perniosis this must also receive attention.

We now have good evidence that faecal flora can be cultured from a high proportion of cases of otitis externa, chronic perionychia and leg ulcers. Have we any readers who could influence the Public Health authorities to re-educate the public in matters of simple hygiene ; to encourage the provision of adequate washing facilities in every water closet, and so reduce the incidence of enteritis and the dermatological conditions cited ?

I am etc.

London, W.1. IAN MARTIN-SCOTT.

BOOK REVIEWS

An African Atlas.*

This is apparently the only work now in print devoted exclusively to dermatology in the negro. A wide range of dermatological conditions is covered by, in the main, excellent black and white photographs with only the briefest descriptions.

The diseases are grouped into sections devoted to those conditions which are more or less the same in white skins, those which are common in European skins but relatively rare in the African, those common in the African and relatively rare in the European, and lastly those conditions found exclusively in the African.

The reviewer is doubtful as to the value of skin atlases in general. A trained dermatologist should have no difficulty in recognizing eruptions in individuals with deeply pigmented skins, and it is felt that even the excellent photographs in this Atlas would not enable the non-dermatologist to unravel any but the simplest problems. More detailed descriptions of the conditions portrayed and guidance on treatment, particularly in hot climates, would be of great value. There is a comprehensive bibliography which is perhaps the most valuable section of this work.

The book is well and pleasingly produced, and in comparison with other similar books, moderately priced.

D.G.F

Smallpox.†

A scholarly composition is always a source of pleasure to the discerning reader, and this description of the 1937–38 epidemic of variola in Hong Kong makes interesting reading indeed. The text is illustrated by excellent black and white plates which depict pyogenic and vascular complications and problems in differential diagnosis as well as recording the various stages in the skin of the morbid process itself. The result is a delightful little monograph which deals concisely but clearly with all aspects of the disease.

A. G. F.

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* *Skin Diseases in the African.* G. H. V. Clarke (1959). London : H. K. Lewis. Pp. 172, illus. 261. Price £4. 4*s*.

† *Variations on a Theme by Sydenham—Small-Pox.* P. B. Wilkinson (1959). Bristol : John Wright and Sons Ltd. Pp. 76. Illus. 68. Price 14*s*. 6*d*.

CURRENT LITERATURE

THE SKIN AND THE MENOPAUSE. D. I. Williams. (1959) *Practitioner*, **182**, 574.

Signs of ageing of the skin may first become obvious at the menopause. On the scalp the hair follicles seem to be fewer in number and less prominent, and diffuse hair loss is frequently seen in mature women. Seborrhoeic warts and skin tags on the neck are common in this age group.

Other conditions discussed include senile angiomas, neurodermatitis, pruritus ani and hyperkeratosis of the heel. R. J. C.

EXPERIMENTAL STUDY OF A GENERALISED FAVUS WITH MULTIPLE SKIN AND GLANDULAR LESIONS. H. Jausion, E. Drouhet, Cl. Nadal, P. Bénard, A. Mazabraud and J. P. Menanteau. (1959) *Ann. Derm. Syph. Paris*, **86**, 137.

A North African man aged twenty-three presented with an almost generalised scaling dermatosis accompanied by suppurating cervical adenitis of sixteen years' duration. *Trichophyton schoenleini* was isolated from all the lesions. Growth in culture was found to depend on vitamin B, in particular pyrimidine. F. F. H.

CHRONIC SWEAT RETENTION WITH RELAPSING URTICATED ERYTHEMA. W. M. Stewart and R. Laumonier. (1959) *Ann. Derm. Syph., Paris*, **86**, 147.

A man of twenty-eight had for a year a rash aggravated by heat and emotion. It consisted of erythematous patches about 1·5 cm. in diameter; sometimes urticated and of irregular outline. Histological evidence is produced to show that blocking of the sweat ducts was the underlying cause. The application of a starch glycerine and salicylic mixture gave rapid relief to his symptoms. F. F. H.

THE IMPORTANCE OF PSYCHOSOMATIC INVESTIGATION IN DERMATOSIS AND THE PRACTICAL DIFFICULTY IN HOSPITAL SERVICE. M. Bolgert and M. Soule. (1959) *Ann. Derm. Syph., Paris*, **86**, 241.

The authors stress the importance of investigating the psychological background in patients with skin diseases. In addition to its importance for diagnosis such an enquiry has a therapeutic action on the patients. They cite three examples in patients with psoriasis, eczema and pruritus. The problem is to find an opportunity for such an investigation in a crowded out-patients, though it is easier with in-patients. Few dermatological assistants however are equipped for such work and even a chief interested in the subject cannot cope with all the problems. The only solution would be the official integration of psychological assistants in the dermatology service. Young dermatologists should be trained along these lines if dermatology is to be given an orientation which at the present time is almost completely lacking in France. F. F. H.

FUNCTIONAL ABNORMALITIES OF SWEAT GLANDS AND PIGMENTATION IN THE FORBEARS. INCONTINENTIA PIGMENTI. X. Vilanova et J. Piñol Aguadé. (1959) *Ann. Derm. Syph., Paris*, **86**, 247.

The authors recall that Franceschelli and Jadassohn subdivided cases of incontinentia pigmenti (i.p.) into two groups. (1) i.p. classica with the characteristic pigmentation preceded by inflammatory lesions, affecting almost exclusively females, transmitted possibly as a recessive and accompanied by ecto- and mesodermal defects. (2) Reticular pigmentary dermatosis without the above classical features and without associated defects elsewhere and inherited as a dominant. They report a baby girl resembling somewhat the former type who showed with her father and his mother a slight palpebral asymmetry also and who they believe really lay between the two groups. The father showed syringomata and an accessory nipple. F. F. H.

THE USE OF THE CHORIOALLANTOIC MEMBRANE OF THE DEVELOPING CHICK FOR CULTURE OF DERMATOPHYTES—A MODIFIED TECHNIC. A PRELIMINARY REPORT UPON ITS USE FOR SERIAL PASSAGE. Betty M. Partridge, (1959) *J. invest. Derm.*, **32**, 605.

The author describes a method for growing fungi on the chorioallantoic membrane of the developing chick. Three strains of *T. rubrum* were studied, the tissue response was similar in all, but the rate at which infection occurred varied. It appears possible that an extension of the methods she described could be utilised to assess the pathogenicity of a given strain of fungus.

A. J.

STUDIES ON THE MODE OF ACTION OF PSORALEN DERIVATIVES. I. THEIR EFFECT ON COPPER AND GLUTATHIONE LEVELS IN BLOOD AND LIVER. A., El-Mofty, A. M., El-Mofty, H., Abdelal, and M. F. S. El-Hawary, (1959) *J. invest. Derm.*, **32**, 645.

The giving of 8-methoxypsoralen in doses of 300–800 mg./kilo body weight to albino rats resulted in an increase in their blood copper levels. No changes were noticed after the exhibition of 5-isoamylene oxypsoralen in similar doses. With 8 methoxypsoralen there was a decrease in the liver glutathione, but there was little change in the blood level of this sulphydryl compound.

It is unfortunate that no estimations of the content of skin glutathione are available, because if this was reduced it would be a possible explanation for the repigmentary action of this psoralen.

A. J.

INJURY AND RE-INJURY TO THE HUMAN EPIDERMIS. II. EPIDERMAL BASAL RESPONSE. D. Brophy and W. C. Lobitz. (1959) *J. invest. Derm.*, **32**, 495.

The epidermis was injured by stripping with scotch tape. The skin was then examined for mitotic activity and for glycogen. There was a sharp rise in the glycogen between 5 minutes and 8 hours with a sudden decrease between 16 and 28 hours.

The effect of repeating the injury at 4 hours, 8 hours, 12 hours, 24 hours, and 48 hours after the initial stripping was investigated. Their studies indicated that in spite of a second injury at progressive intervals up to 48 hours the responses demonstrated were those due to the first injury. Glycogen after the second stripping showed little difference from that of the control; the mitotic activity also appeared to be related to the first insult. A. J.

BIOASSAY OF NATURAL AND SYNTHETIC FUROCOUMARINS (PSORALENS). M. A. Pathak and T. B. Fitzpatrick. (1959) *J. invest. Derm.*, **32**, 509.

Substances of the furocoumarin group were tested on guinea pig and human skin for their erythema producing and pigmenting abilities. Of 18 compounds examined psoralen itself, and its three methyl derivatives were found to be the most active.

They found that fused coumarin and furan rings (as found in the psoralen molecule) was essential for photodynamic action; either ring formation alone was not effective. A. J.

THE SYSTEMIC AND LOCAL TREATMENT OF EXPERIMENTAL DERMATOPHYTOSIS WITH GRISEOFULVIN. A. R. Martin. (1959) *J. invest. Derm.*, **32**, 525.

This author reports the successful treatment with Griseofulvin of experimentally induced *T. mentogryphytes* infections in guinea pigs. The antibiotic was effective locally in a concentration of 1%, but the effect was much better when given orally in doses of 25–100 mg./Kg. daily for 8 days. A. J.

ALTERED L-METHIONINE S^{35} UTILIZATION IN PSORIASIS. M. J. Lipnik and H. S. Levy. (1959) *J. invest. Derm.*, **32**, 519.

These workers compared the S^{35} uptake by psoriatic skin, unaffected skin of psoriatic patients, and control normal skin. After a single oral dose of 40 μc. of radioactive sulphur labelled L-methionine, the activity of the skin was measured by placing a Geiger tube over the site to be investigated; the psoriatic scales were removed daily.

Psoriatic plaques had a much greater uptake and retention of radioactive sulphur than either normal skin or unaffected skin of psoriatics. They therefore suggested that there was a defective sulphur metabolism in psoriasis. However, sulphydryl containing substances play an important part in cell metabolism, and the results obtained may merely reflect the great epidermal activity present in this condition rather than any specific enzymatic disturbance. A. J.